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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/441,355 05/15/95 HOUGHTON

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EXAMINER

CHIRON CORPORATION
INTELLECTUAL PROPERTY - R440
P.O. BOX 8097
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ZEMAN, M

ART UNIT

PAPER NUMBER

1631

DATE MAILED:

08/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

08/441,355

Applicant(s)

HOUGHTON ET AL.

Examiner

Mary Zeman

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 115-182 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 115-182 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 29.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's second submission after final filed on 11/17/00 has been entered.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1631**. Claims 115-182 are pending in this application. The amendments filed on the following dates have each been entered: 1/26/01, 4/3/01, and 5/31/01. The summation of these amendments resulted in the cancellation of claims 88-104 and 106-114, the amendment of claims 115-127, 138, 144, and 154-161, and the addition of claims 162-182. The Associate Power of Attorney, filed 11/17/00, and the Change of Address, filed 4/25/01, have been entered. The IDS filed 8/6/01 has also been entered and considered.

Drawings

Applicant is required to submit a proposed drawing correction in reply to this Office action. Due to changes in procedure, formal correction of the noted defect **can no longer be deferred** until the application is allowed by the examiner.

Claim Objections

Claims 154-161 and 164-182 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 154-157, 167 set forth that the selected samples are "for use in passive immunotherapy" which is not a positive active method step further limiting the methods of claims 132, 133, 138, 142 and 144. This is an intended use limitation does not further limit the claimed methods. Claims 158-161 set forth that the selected samples are "for use in the preparation of polyclonal antibodies" which is not a positive active method step further limiting the methods of claims 132, 133, 138 and 142. Claims 164-166, 168-

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182 recite that the selecting is done to identify a sample for removal from the supply. This is not a positive active method step further limiting the claims from which they depend. This is an intended use, and not a limitation of the method itself.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 115-182 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 115-182 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are as follows.

In claim 115, the method of selecting samples, comprising selecting samples that contain a detectable polynucleotide fail to set forth any detection steps such that samples that do contain the polynucleotide can be selected, and those which do not, are not.

Similar problems exist in claims 116, 117.

In claim 118, the method of selecting samples comprising selecting samples comprising either a polynucleotide or an antibody to an HCV polypeptide, fails to set forth any detection steps of the polynucleotide or antibodies such that appropriate samples can be selected.

Similar problems exist for claims 119-129, 162, 163.

Claims 130-182 depend from the above rejected claims, and therefore are also indefinite.

Claims 150-153, 167 recite the limitation "samples that are not selected..." in reference to claim 132, and others. There is insufficient antecedent basis for this limitation in the claim. There is no basis in the claims from which claims 150-153, 167 depend for identifying and/or using samples that are NOT selected.

In claims 158-161, it is unclear that all the samples identified by the methods of claims 115-125, 162 or 163 etc. would comprise antibodies which would be useful in the preparation of polyclonal antibodies. It would seem that only samples wherein such antibodies had been

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detected would be useful in this regard. Claims 115-117, for example, detect only polynucleotides, and do not select on the basis of the presence of antibodies in the sample.

Similarly with claims 154-157, it would appear that only samples wherein HCV-specific antibodies had been detected would be useful in passive immunotherapy. Passive immunotherapy is a transfer of humoral immunity by administering an antibody fraction of sera of infected patients. It would seem that only samples wherein such antibodies had been detected would be useful in this regard. Claims 115-117, for example, detect only polynucleotides, and do not select on the basis of the presence of antibodies in the sample.

Claims 154-157 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to methods of selecting samples which contain or comprise HCV polynucleotides or antibodies to HCV antigens, wherein the selected samples are for use in passive immunotherapy. The specification, as filed, is not enabling for these claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must identify and use polyclonal antibodies or anti-HCV antibodies in passive immunization methods. For the reasons discussed below, there would be an unpredictable and undue amount of experimentation required to practice the claimed invention.

b) The specification provides guidance for methods of detecting HCV polynucleotides, and antibodies to HCV antigens in patient samples. The specification also mentions that these detection assays can be used to screen blood banks, to identify samples for further study of HCV, to identify samples having antibodies which can be combined and purified to create a mixture of

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polyclonal antibodies, etc. At page 60 of the specification, the specification notes that it is neutralizing antibodies that are useful in passive immunotherapy methods. The specification does not set forth how to identify, or make neutralizing antibodies of HCV.

c) The specification provides no working examples detecting samples comprising anti-HCV antibodies, and then using them in passive immunotherapy experiments.

d) The invention is drawn to methods of selecting particular samples which comprise anti-HCV antibodies for use in passive immunotherapy.

e) State of the art, The term "passive immunotherapy" or "passive immunity" has a standard definition in the art of Immunology, which is: "A resistance to disease or infection acquired by an individual through the transfer of antibodies from an immune donor to a nonimmune recipient, or through the transfer of maternal antibodies to a fetus." (Academic Press Dictionary of Science and Technology Online: www.harcourt.com/dictionary 2001)

The specification, as filed fails to demonstrate that any samples comprising anti-HCV antibodies that would be selected by the claimed methods would have any use in passive immunotherapy methods.

HCV, a flavivirus, is known to be a highly variable virus upon infection of an appropriate host. HCV uses reverse transcription in its life cycle, which is an imperfect process leading to the existence of viral Quasispecies all having slightly differing sequences and properties. The virus is easily able to adapt and work around the host immune response because of this variability. These types of adaptations and mutations are known as escape mutants. It is well known in the art that viruses that are highly adaptable in vivo are generally highly resistant to eradication and/or prevention by passive immunotherapeutic methods. (Fields, ED. Fundamental Virology, Second Edition, Raven Press, New York, 1991, pages 245-249). The specification does acknowledge that other species or strains may exist, but does not address these other species in the context of how to perform effective passive immunotherapeutic methods. The specification does not identify any particular antigens or epitopes as being the target of neutralizing antibodies such that one of skill in the art could test antibody preparations for reactivity with that epitope. The specification does not set forth a viable viral replication assay wherein the samples could be tested for their ability to block infection of relevant target cells.

f) The skill of those in the art of molecular biology is high.

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g) The prior art predicts that passive immunity for protection from HCV will be ineffective.

h) The claims are broad because they are drawn to methods of using any sample comprising anti-HCV antibodies for passive immunotherapy.

The skilled practitioner would first turn to the instant specification for guidance to practice methods of detecting, selecting and using samples comprising anti-HCV antibodies for passive immunotherapy. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that the success of such passive immunotherapy experiments or tests are not expected to be successful in the prevention of HCV infection. Finally, said practitioner would turn to trial and error experimentation to determine what specific antibodies would be useful in attempting to block HCV infection and replication. Such further research and experimentation clearly represents undue experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 118, 119, 123-125, 129-132, 136- 138, 142- 144, 148- 150, 152, 154-158, 160, 161, 164, 167, 169, 170, 171, 175-177, 181, 182 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 5,350,671. Although the conflicting claims are not identical, they are not patentably distinct

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from each other because the method of the patent is specifically for detecting the presence of antibodies that bind HCV antigens. This test performs the same method steps and has the same inherent use of screening a blood bank, or selecting particular samples because they contain HCV-specific antibodies.

The claims of the instant application are drawn to methods of selecting human samples from a supply of samples which comprise antibodies which bind HCV epitopes. No particular detecting methods are set forth in the claim, but the specification discloses immunoassays for HCV-specific antibodies. The selection is done to select samples for various intended uses: for passive immunotherapy, for preparation of polyclonal antibodies, for production of blood-products. These are merely intended use limitations which do not further limit any of the method steps.

The immunoassay of the Patent (5,350,671) detects the presence of HCV-specific antibodies in samples from human patients, in order to identify and select those samples which react, and to identify which samples do not react. Samples which do not react would appear to be free of HCV infection. The detection assay can be done with blood, plasma or serum (claim 3), the antigen can be made recombinantly (claim 2), the antigen to which the antibody reacts can be from Figure 90 (claims 10-21) or the same ATCC deposit (claim 1) recited in the instant claims.

This immunoassay was developed for the purpose of screening a supply of blood products in order to select out HCV+ samples, and to retain HCV- samples. The screening of donated blood products for the presence of known pathogens was well known in the art at the time of the invention, as evidenced by Seto (4,707,439) who provides a screening test for detecting the presence of an infectious agent that putatively causes non-A non-B hepatitis, or AIDS. A particular property of a pathogen (RT activity) is measured in a supply of samples in order to select those that are positive for viral contamination and to retain samples which are not contaminated with the pathogen.

In addressing the issue of intended use, the CAFC has stated that the intended use language in a method claim is non-limiting when the methods utilize the same method steps. (Bristol-Meyers Squibb. Co. vs. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001)) Here, the detecting step of the instant claim appears to be performed with the same methods of

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the cited patent. The language of the preamble does not result in a manipulative difference in the steps of the claim. Further, the claimed process is not drawn to a new use: the immunoassay of the patent is directed to the same method of selecting a sample that contains antibodies against HCV.

Claims 115-122, 126, 127, 128, 132-135, 138-141, 144-147, 151-156, 158-160, 162-166, 168, 171-174, 177-180 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,863,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of the patent is specifically for detecting the presence of HCV specific polynucleotides. This test performs the same method steps and has the same inherent use of screening a blood bank, or selecting particular samples because they contain HCV-specific polynucleotides..

The claims of the instant application are drawn to methods of selecting human samples from a supply of samples which comprise HCV specific polynucleotides, or polynucleotides that hybridize to an HCV genome under stringent conditions. No particular detecting methods are set forth in the claim, but the specification discloses methods of using sections of HCV genome, DNA from the deposit, and DNA from the figures as probes for detecting HCV-specific sequences. The selection is done to select samples for various intended uses: for the cloning of more HCV sequences, for the detection of HCV in a sample, etc. These are merely intended use limitations which do not further limit any of the method steps.

The hybridization based assay of the Patent (5,863,719) detects the presence of HCV-specific polynucleotides in samples from human patients, in order to identify and select those samples which react, and to identify which samples do not react. Samples which do not react would appear to be free of HCV infection. The detection assay can be done with blood, plasma or.

This assay was developed for the purpose of screening a supply of blood products in order to select out HCV+ samples, and to retain HCV- samples. The screening of donated blood products for the presence of known pathogens was well known in the art at the time of the invention, as evidenced by Seto (4,707,439) who provides a screening test for detecting the presence of an infectious agent that putatively causes non-A non-B hepatitis, or AIDS. A

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particular property of a pathogen (RT activity) is measured in a supply of samples in order to select those that are positive for viral contamination and to retain samples which are not contaminated with the pathogen.

In addressing the issue of intended use, the CAFC has stated that the intended use language in a method claim is non-limiting when the methods utilize the same method steps. (Brystol-Meyers Squibb. Co. vs. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001)) Here, the detecting step of the instant claim appears to be performed with the same methods of the cited patent. The language of the preamble does not result in a manipulative difference in the steps of the claim. Further, the claimed process is not drawn to a new use: the assay of the patent is directed to the same method of selecting a sample that contains HCV sequences.

Claims 118, 119, 123-125, 129-132, 136- 138, 142- 144, 148- 150, 152, 154-158, 160, 161, 164, 167, 169, 170, 171, 175-177, 181, 182 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-64 of U.S. Patent No. 5,698,390. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of the patent is specifically for detecting the presence of antibodies that bind HCV antigens. This test performs the same method steps and has the same inherent use of screening a blood bank, or selecting particular samples because they contain HCV-specific antibodies.

The claims of the instant application are drawn to methods of selecting human samples from a supply of samples which comprise antibodies which bind HCV epitopes. No particular detecting methods are set forth in the claim, but the specification discloses immunoassays for HCV-specific antibodies. The selection is done to select samples for various intended uses: for passive immunotherapy, for preparation of polyclonal antibodies, for production of blood-products. These are merely intended use limitations which do not further limit any of the method steps.

The immunoassay of the Patent (5698390) detects the presence of HCV-specific antibodies in samples from human patients, in order to identify and select those samples which react, and to identify which samples do not react. Samples which do not react would appear to

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be free of HCV infection. The detection assay can be done with blood, plasma or serum (claim 2), the antigen can be made recombinantly (claim 4), the antigen to which the antibody reacts can be from Figures 90, 47, 14, 66 (claims 8-11) or the same ATCC deposit (claim 12) recited in the instant claims.

This immunoassay was developed for the purpose of screening a supply of blood products in order to select out HCV+ samples, and to retain HCV- samples. The screening of donated blood products for the presence of known pathogens was well known in the art at the time of the invention, as evidenced by Seto (4,707,439) who provides a screening test for detecting the presence of an infectious agent that putatively causes non-A non-B hepatitis, or AIDS. A particular property of a pathogen (RT activity) is measured in a supply of samples in order to select those that are positive for viral contamination and to retain samples which are not contaminated with the pathogen.

In addressing the issue of intended use, the CAFC has stated that the intended use language in a method claim is non-limiting when the methods utilize the same method steps. (Bristol-Meyers Squibb. Co. vs. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001)) Here, the detecting step of the instant claim appears to be performed with the same methods of the cited patent. The language of the preamble does not result in a manipulative difference in the steps of the claim. Further, the claimed process is not drawn to a new use: the immunoassay of the patent is directed to the same method of selecting a sample that contains antibodies against HCV.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

The official fax number for this Art Unit is (703) 308-4242. An unofficial fax number, direct to the Examiner is 703 746 5279. Please call prior to use of this number.


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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose telephone number is (703) 305-3524.

mkz
8/9/01


MARY K. ZEMAN
PATENT EXAMINER
(1063)